Original Article

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Clinical Profile of Hypoxic- Ischemic Encephalopathy in Neonates with Birth Asphyxia in a Rural Tertiary Care Hospital in Central India

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Abstract

Context- Perinatal asphyxia and Postasphyxial hypoxic-ischemic encephalopathy (HIE) is a major cause of early neonatal mortality in India accounting for 24.3% of neonatal deaths. *Aim*- To study risk factors, clinical, biochemical, Neurosonography parameters and short term outcome of neonates with HIE. *Setting and Design*- Study conducted at AVBRH, Sawangi (M) after seeking IEC approval. It was a prospective observational study. *Material and method*-All neonates delivered in AVBRH and admitted to NICU with birth asphyxia and HIE were included in the study. A detailed history, examination, HIE staging, cord blood ABG, Neurosonography, other investigations and short term outcome were recorded in prevalidated proforma and data was statistically analyzed using SPSS 22.0. *Results*- Incidence of Birth asphyxia was 2.97%, incidence of HIE was 1.76%. Of all neonates with HIE (study group n=50) 26% were in HIE stage I, 54% were in stage II and 20% were in stage III. On umbilical cord ABG 20% neonates had severe acidemia and 80% had moderate acidemia. Neurosonography changes were seen in 4% neonates, mortality rate was 18%. All 9 neonates who died were in HIE stage III. *Conclusion*-Birth asphyxia and HIE are still a major cause of neonatal morbidity and mortality. HIE stage III, severe acidemia are associated with high mortality. Preclampsia, oligohydramnios and MSAF are risk factors associated with HIE.

Keywords: Birth Asphyxia; HIE; Incidence; Mortality and Risk Factors.

Introduction

India contributes to one-fifth of global live births and more than a quarter of neonatal deaths [1]. The neonatal mortality rate (NMR) in India was 28 per 1000 live births with perinatal mortality rate (PMR) of 26 per 1000 births and the early NMR of 22 per 1000 live births in 2013. Deaths in the first week alone account for approximately 45% of total under-five deaths [2].

The true burden of birth asphyxia is difficult to estimate because of the different definitions used in the studies. According to World Health Organization (WHO) in the developing countries 3% of all infants suffer from moderate to severe birth asphyxia, of which 23% die and approximately the same numbers develop serious sequelae. Asphyxia accounts for 23% of neonatal deaths globally, and 8% of all deaths in children under five years of age [3].

Birth asphyxia is the cause of 20% of neonatal deaths in India. About 2.8 and 5.6% of all live births had moderate and severe asphyxia, respectively, in a large hospital-based study; the case fatality rate was relatively low at ~8.7% [4].

Perinatal asphyxia is one of the major causes of early neonatal mortality in India. Among the institutional births, incidence is 5% and accounts for 24.3% of neonatal deaths [5].

Postasphyxial Hypoxic Ischemic Encephalopathy (HIE) occurs in approximately 1 to 2 infants per 1000 live term births in developed countries but in developing countries its incidence is expected to be much higher [6]. Among term infants, 6% to 23%of cases of cerebralpalsy (CP) are attributable to intrapartum asphyxia [7]. Predictions of long-term

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out come in the immediate neonatal period are based on clinical, biochemical, electrophysiological and imaging findings.

HIE is characterized by clinical and laboratory evidence of acute or subacute brain injury due to asphyxia.

Systemic hypoxemia and/or reduced cerebral blood flow (CBF) in utero or postnatally are primary causes of HIE.

Perinatal asphyxia is an insult to fetus or newborn due to lack of oxygen (hypoxia) or lack of perfusion (ischemia) to various organs of sufficient magnitude and duration.

In a study conducted at Thailand, significant risk factors for HIE were inappropriate antenatal care, vacuum extraction, male sex, prolapsed cord and 1 and 5-minute low Apgar scores [8].

In HIE neonate may have low Apgar scores at delivery and metabolic acidosis is documented in the cord blood. Within the first 24 hours of life, the infant may develop symptoms of apnea and seizures. Neurosongraphy (NSG) provides a convenient, non invasive screening examination of the hemodynamically unstable neonate at the bedside. NSG findings suggestive of HIE include hyperechogenicity of involved structures and/or abnormal Resistive Index (RI) on duplex Doppler images. But NSG is operator dependent and less sensitive to structural abnormalities in the cerebral convexity and in the brainstem.CT brain is the least sensitive modality for evaluation of HIE and most sensitive and specific is MR imaging, diffusion-weighted MR imaging and MR spectroscopy [9].

Perinatal asphyxia and HIE are still a major contributor to neonatal mortality and morbidity irrespective of improved obstetric and perinatal care. In view of paucity of studies on perinatal asphyxia and HIE in central rural India this study was undertaken with following objectives:

1. To study clinical, biochemical and NSG parameters of neonates with HIE.
2. To study the risk factors for HIE.
3. To study the short term outcome of neonates with HIE.

Materials and Method

After seeking approval from IEC (Ref.No. DMIMS (DU) / IEC/2016-15/5099) this study was undertaken in NICU (Inborn), Department of Pediatrics AVBRH, Sawangi (M), Wardha. It was a prospective observational case study conducted from December 2016 to December 2017. All neonates delivered in our hospital and admitted to NICU (Inborn) with birth asphyxia and HIE were included in the study.

The neonates included in study fulfilled following criteria [10,11]:

1. Moderate birth asphyxia: Slow/gasping breathing or an Apgar score of 4 to 6 at 1 minute
2. Severe birth asphyxia: No breathing or an Apgar score of 0-3 at 1 minute of age
3. Umbilical cord blood gas analysis within 1st hour of birthwith ph <7.2
4. HIE stage I, II & III according to Sarnath & Sarnath clinical staging of HIE [12].

Exclusion Criteria

1. Neonates with congenital malformations, infections, chromosomal abnormalities, inborn errors of metabolism, dysmorphic syndromes and still born.
2. Neonates who died or were discharged within 24 hours of birth.

A detailed maternal obstetric history was taken in a predesigned prevalidated proforma, to assess the role of maternal factors along with detailed history and examination of all neonates included in the study. The neonates were assessed and followed closely to assign a stage of HIE as stageI, II and III (mild, moderate and severe) according to the Sarnat and Sarnat clinical staging of HIE. The clinical course, complete blood count (CBC), C- reactive protein (CRP), Blood culture along with cord blood pH and gases and NSG were done and reports were entered in the pre-validated proforma. On discharge, babies were assessed for abnormal neurological signs like tone abnormalities, Moros reflex, feeding difficulty. The short term outcome and condition of neonates at discharge were noted. Birth asphyxia was considered to be severe if cord blood pH was < 7.

Statistical analysis were performed on Microsoft excel and SPSS software. Data was summarized using descriptive statistics. Categorical variables are presented as number and percentage. Chi-square test was used to compare the association among two or more categorical variables. All statistical tests were two-tailed and alpha level of significance was set less than 5%. A p value of <0.05 was taken as statistically significant.

Results

Total number of live births in our hospital during study period were 2830, out of them 84 (2.97%) neonates had birth asphyxia that is incidence of birth asphyxia was 29.7 per 1000 live births.Out of 2830 live births 50 (1.76%) had HIE which means 17.6 per 1000 live births was incidence of HIE. Birth asphyxia accounted for 14.7% of admissions to NICU, out of 571 admissions in inborn NICU 84 had birth asphyxia.Out of 84 birth asphyxia neonates 50 (59.5%) developed HIE (Table 1 Graph 1).

Out of 2830 live births 1367 (48.3%) were normal vaginal deliveries (NVD) and 1463 (51.7%) were lower segment cesarean section (LSCS). In the study group 50 neonates with HIE were included, 32 (64%) were males and 18 (36%) were females with M:F ratio of 1.8:1, of the study group 26 (52%) were born by LSCS and 24 (48%) were born by NVD.

In study group 35 (70%) were full term (FT), 15 (30%) were preterm, 30 FT were AGA, 5 were SGA and all 15 preterm neonates were AGA thus 90% were AGA and 10% were SGA.

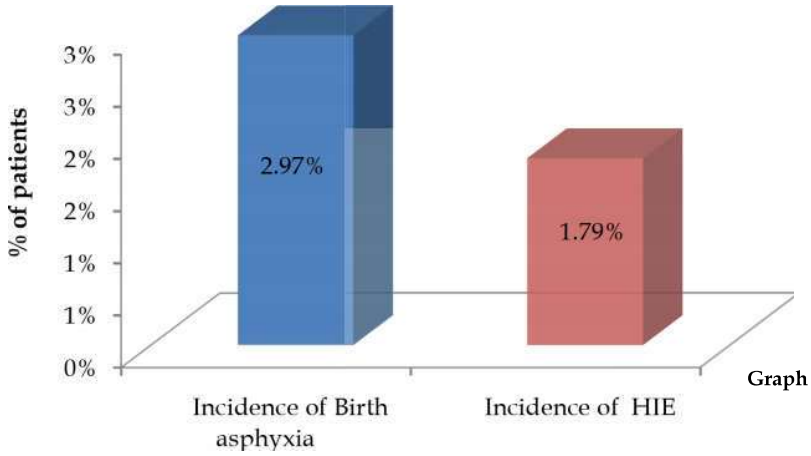
In cases maternal risk factors associated were, 5 (10%) had preeclampsia, 5 (10%) had oligohydramnios, 4 (8%) had meconium stained amniotic fluid (MSAF), 2 (4%) had polyhydramnios, 2 (4%) had gestational diabetes mellitus (GDM), 2 (4%) mothers had severe anemia, 1 (2%) had premature rupture of membranes (PROM)> 12 hours and 1 (2%) had prolonged labor.

Out of 50 neonates with HIE 13 (26%) were in stage I, 27 (54%) were in stage II and 10 (20%) were in stage III. Umbilical cord ph showed that 10 (20%) neonates had severe acidemia and 40 (80%) had moderate acidemia. Out of 10 neonates with severe acidemia 5 (50%) died. In 20 (40%) cases CRP was positive and blood culture was positive in 6 (12%) of cases. NSG changes were seen in 2 (4%) neonates, out of 2 neonates with mild prominence of bilateral lateral ventricles on NSG one died. In short term outcome 41 (82%) were discharged and 9 (18%) died, mortality rate was 18%. All 9 neonates who died were in HIE stage III. One newborn with HIE stage III was discharged,in neonates with HIE stage II out of 27 neonates 13 had good cry, tone activity at discharge and 14 had fair cry tone activity at discharge. All 13 cases with HIE stage I at discharge had good cry, tone and activity. Out of these 9 deaths 3 (33%) neonates had associated culture positive sepsis of which 2 (66%) had

Table 1: Incidence of Birth Asphyxia & HIE

Variables	Frequencies
Live births during study period	2830
Neonates with Birth asphyxia	84 (2.97%)
Neonates with HIE secondary to birth asphyxia and admitted to NICU (study population)	50 (1.76%)
Incidence of Birth asphyxia	29.7/1000 live births or 2.97%
Incidence of HIE	17.6/1000 live births or 1.76%

Abbreviations: HIE- Hypoxic Ischemic Encephalopathy
NICU- Neonatal Intensive Care Unit



Graph 1: Incidence of Birth Asphyxia & HIE-

Table 2: Clinical Profile of HIE associated with Birth Asphyxia

	Number	Percentage
Sex		
Male	32	64%
Female	18	36%
Mode of Delivery		
NVD	24	48%
LSCS	26	52%
Gestational age		
SGA	5	10%
AGA	45	90%
Risk factors		
MSAF	4	8%
Preeclampsia	6	12%
Oligohydramnios	5	10%
Polyhydramnios	2	4%
GDM	2	4%
Severe Anemia	2	4%
PROM>12 hrs	1	2%
HIE Stages (Sarnath & Sarnath)		
HIE Stage I	13	26%
HIE Stage II	27	54%
HIE Stage III	10	20%
Umbilical cord blood pH		
pH 7 to 7.2	40	80%
pH < 7	10	20%
NSG		
Normal	48	96%
Abnormal	2	4%

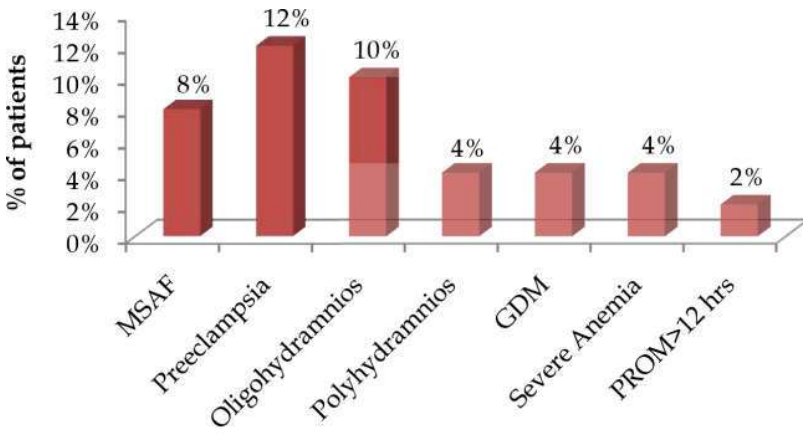
Abbreviations:
NVD- Normal Vaginal Delivery
LSCS- Lower Segment Cesarean Section
SGA- Small for Gestational Age
AGA- Appropriate for Gestational Age
MSAF- Meconium Stained Amniotic Fluid
GDM- Gestational Diabetes Mellitus
PROM- Premature Rupture of Membranes
HIE- Hypoxic Ischemic Encephalopathy
NSG- Neurosonography

Pseudomonas and 1 (33%) had Kleibsiella in their blood culture (Table 2 Graph 2).

When the two groups discharged and expired were compared there was no significant difference between the two groups regarding gender, parity, gestational age and maternal risk factors (p value>0.05). But there was significant difference in staging of HIE and short term outcome, all neonates in expired group were in HIE stage III and all those who were discharged were in HIE stage I and II (p value = 0.0001, S).

Severe acidemia in cord blood (pH<7) was associated with increased mortality and moderate acidemia (pH 7 -7.2) neonates had better short term outcome (p=0.0032, S).

Anemia and high mortality had significant correlation (p=0.0009, S) and positive blood culture also was associated with mortality (p=0.029, S) (Table 3 Graph 3).

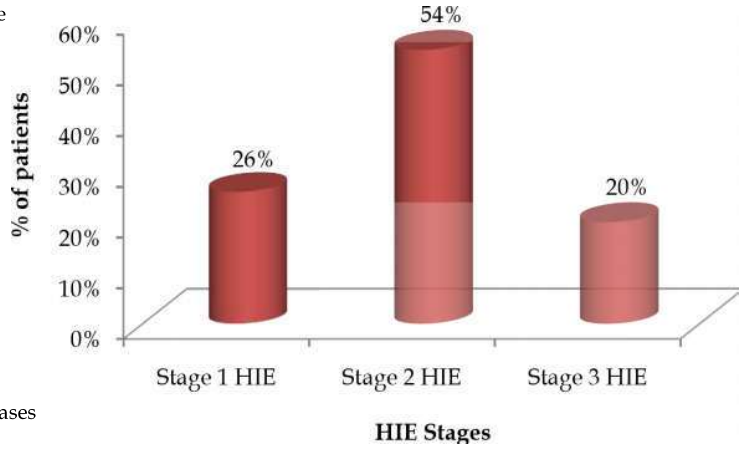


Graph 2: Maternal Risk factors in HIE with birth asphyxia

Table 3: Risk factors, HIE staging, clinical profile and their distribution in 2 groups (Discharged & Expired)

	Discharged (n=41)	Expired n=9)	p- value
Gender	24	6	0.94,NS
Male	17	3	
Female			
Parity	22	4	0.61,NS
Primipara	19	5	
Multipara			
Gestational Age	28	7	0.57,NS
Full Term	13	2	
Preterm			
Maternal Risk factors-			
MSAF	3	1	0.56,NS
Pre-eclampsia	5	1	1.00,NS
Oligohydramnios	3	2	0.21,NS
Polyhydramnios	1	1	0.33,NS
GDM	2	0	1.00,NS
Severe Anemia	1	1	0.33,NS
PROM>12 hrs	1	0	1.00,NS
Prolonged Labour	0	1	0.18,NS
HIE Stage I	13	0	**0.0001,S**
HIE Stage II	27	0	
HIE Stage III	1	9	
Umbilical cord blood pH			
pH 7 to 7.2	36	4	**0.0032,S**
pH < 7	5	5	
NSG			
Normal	40	8	0.22,NS
Abnormal	1	1	
Hb%	2	4	
Anemia (Hb% < or = 13.6 gm %)	4	0	
Septic screen	0	0	**0.0009,S**
Leucopenia (< 9000/ mm^3)	7	2	0.23,NS
Leucocytosis (> 30,000/mm^3)	1	0	**0.029,S**
Thrombocytopenia (<1,50,000	14	6	
Thrombocytosis (> 4,00,000	3	3	
CRP	(Micrococci-2	(Psuedomonas-2	
Blood Culture	Psuedomonas-1)	Kliebsiella-1)	

Abbreviations: MSAF- Meconium Stained Amniotic Fluid
GDM- Gestational Diabetes Mellitus
PROM- Premature Rupture of Membranes
HIE- Hypoxic Ischemic Encephalopathy
NSG- Neurosonography
Hb%- Hemoglobin percentage
CRP- C Reactive Protein



Graph 3: Staging of HIE in cases

Discussion

This study was undertaken to know the clinical, biochemical and neurosonographic parameters, risk factors and short term outcomes of neonates with HIE secondary to birth asphyxia in NICU of our hospital. The study group consisted of 50 neonates with HIE secondary to birth asphyxia admitted in inborn NICU over a period of 12 months. The incidence of birth asphyxia was 29.7 per 1000 live births or 2.97%. The incidence of HIE secondary to birth asphyxia was 17.6 per 1000 live births or 1.76%. This was similar to a study by Bhunia NS [13] in which incidence rate of perinatal asphyxia and HIE was 28.5 /1000 live births and 19.97/1000 term live births respectively. Padayachee N [14] in his study found that incidence of perinatal asphyxia was 4.7/1000 live births, and that of HIE was 3.6/ 1000 live births which was much less as compared to this study.In Siva Saranappa SB [15] study frequency of perinatal asphyxia was 5.1% which was slightly high than our study and this could be due to inclusion of neonates born outside their hospital and referred within one hour of birth. However this incidence does not reflect the true incidence as most of the data were hospital based and was of single centre, which does not reflects the true incidence in general population. In this study 59.5% of birth asphyxia neonates developed HIE these findings are similar to study by Lohan R [16] in which 42% of birth asphyxia neonates developed HIE but in study bySiva Saranappa SB [15] 31.66% developed HIE, whereas in a study by Thakkar PA [17] 77.7% of full term neonates with severe birth asphyxia developed HIE and 83% developed HIE of all full term birth asphyxia cases in study byBhunia NS [13] which are not similar to our findings. In this study according to Sarnath & Sarnath staging for HIE 26% were in HIE stage I, 54% were in HIE stage II & 20% in HIE stage III this distribution was not similar to study by Lohan R [16] where 23.81% were HIE-I, 33.33% HIE-II and 42.86% HIE-III and in study by Bhunia NS [13] 43.42% cases were in Stage I HIE, 28.07% were in stage II HIE and 28.91% were in stage III HIE.

Maternal risk factorsassociated with birth asphyxia were preclampsia, oligohydramnios, meconium stained liquor but were not statistically significant.Thakkar PA [17] in his study found that maternal risk factors associated with increased neonatal mortality were prolonged labour, oligohydramnios, polyhydramnios and severe anaemia. Whereas MSAF was significant risk factor associated in study by Siva Saranappa SB [15] and in study by Bhunia NS [13] prolonged labour, primiparity, fetal distress were significant risk factor.

In this study 20% neonates had severe acidemia (pH<7) and 50% of these neonates expired, 88% of discharged neonates had moderate acidemia (pH 7-7.2) and these findings were statistically significant. Siva Saranappa SB [15] study 35% had severe acidemia and out of them 23.8% expired.

In this study overall mortality rate was 18% which is similar to Padayachee N [14] in which overall mortality rate was 13.3% and to study by Lohan R[16] in which overall mortality was 14%but it was higher the Siva Saranappa SB [15] study in which overall mortality rate was 8% but was less as compared with Bhunia NS [13] study in which overall mortality rate was 31%. Mortality was higher in HIE III which was 90% whereas in HIE stage I & II there was no mortality in present study and these findings are similar to Bhunia NS [13] study where in HIE stage III mortality was 93.84% and in HIE II it was 15.62% and in Siva Saranappa SB [15] study mortality in HIE stage III neonates was 100%.

Conclusion

Birth asphyxia and HIE still are one of the major causes for admission of neonates to NICU and one of the leading causes which contribute to early neonatal mortality and morbidity. Stringent monitoring for well being of mother and baby throughout entire pre-conceptional and antenatal period right through labour and during early neonatal period with early efficient management will definitely help to further reduce the incidence of HIE and will improve the outcome of these newborns. Further research is needed for monitoring, diagnosis and newer modalities of treatment for HIE in neonates and more long term follow up studies should be undertaken in future.

Acknowledgement

Nil

Conflict of Interest: Nil

Key Message

Birth asphyxia and HIE are still a major cause of neonatal morbidity and mortality, research should be undertaken in preventive and treatment modalities for HIE and Birth Asphyxia.

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